UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,602	03/21/2001	Petros Karouzakis	1581/128WO	6697

2101 7590 08/18/2004

BROMBERG & SUNSTEIN LLP
125 SUMMER STREET
BOSTON, MA 02110-1618

EXAMINER	
HUI SAN MING R	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 08/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,602	KAROUZAKIS ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-31,33-42 and 48-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-31, 33-42, and 48-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 7, 2004 has been entered.

The cancellation of claims 32, 43-47 is acknowledged. The addition of claims 55-58 is also acknowledged.

Claims 27-31, 33-42, and 48-58 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 58 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The recitation "other than a histamine or histamine receptor agonist" recited in claim

58 is supported by the originally filed specification and claims. Applicant is required to cancel such recitation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 27-31, 33-42, and 48-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nahoum (US Patent 5,773,457) in view of El-Rashidy (US Patent 5,256,652), Lowrey (US Patent 5,981,563) and Reilly (chapter 80 in Remington: The Science and Practice of Pharmacy, page 1397, 1509-1512), references of record in the previous office action mailed May 23, 2001. Reasons for the rejection are essentially the same as that set forth in the previous office action mailed May 23, 2001.

Nahoum teaches that a composition containing both misoprostol (a prostaglandin E_1 analog) and alprostadil (a prostaglandin E_1) are useful in treating female sexual dysfunction (See col. 9, lines 47-48; lines 53- col.10, line 1). Nahoum also teaches that the female sexual dysfunction treating composition, which may contain misoprostol, can be administered topically as gel, cream or ointment (See particularly col. 10, line 48-49). Nahoum also teaches that penetration enhancing agent may be incorporate into the female

sexual dysfunction treating composition, which may contain misoprostol (See col. 14, line 8 - col. 15, line 48).

Nahoum does not expressly teach that the topical sexual dsyfunction treating composition employs misoprostol or misoprostol and alprostadil in combination particularly. Nahoum does not expressly teach that the amount of misoprostol to be 0.3-0.9%. Nahoum does not expressly teach the application of the topical prostaglandin composition in a method of treating female sexual dysfuntion to the vagina or clitoris. Nahoum does not expressly teach the female sexual dsyfunction treating method comprising α-cyclodextrin, gelatin, and hydroxymethylcellulose. Nahoum does not expressly teach the female sexual dsyfunction treating method comprising hydroxypropyl methylcellulose which comprises hydroxypropyl methylcellulose 3000 in the amount of 4% w/v.

El-Rashidy teaches a topical sexual dysfunction treating composition that comprises a vasodilating agent, α-cyclodextrin, and hydroxypropyl methylcellulose (See col. 3, line 67-68; col. 6, line 2-4). El-Rashidy also teaches that the amount of hydroxypropyl methylcellulose is 2-3%w/v (See col.8, Table II).

Lowrey teaches that the sexual response in females involve vasodilation and engorgement of the genitalia with arterial blood in a manner analogous to the male erectile response (See col. 5, line 38-51).

Reilly teaches that gelatin is useful as an emulsifying agent which can be utilized to formulate topical formulation (page 1397, col. 1; also page 1510 col.1, last paragraph).

It would have been obvious for one of ordinary skill in the art at the time the invention was made to apply a topical female sexual dysfunction treating composition of misoprostol in the amount of 0.3-0.9% with or without the second vasoactive agent onto the vagina or clitoris. It would have been obvious for one of ordinary skill in the art at the time the invention was made to incorporate α-cyclodextrin, gelatin, and hydroxyproopyl methylcellulose, which comprises hydroxypropyl methylcellulose 3000 in the amount of 4%, into the topical female sexual dysfunction treating composition in a method to treat female sexual dysfunction.

One of ordinary skill in the art would have been motivated to apply the sexual dsyfunction treating composition, employing misoprostol in the amount of 0.3-0.9%, with or without another vasodilator, cyclodextrin, gelatin, and hydroxypropyl methylcellulose, which comprises hydroxypropyl methylcellulose 3000 in the amount of 4%, onto the vagina or clitoris in a method to treat female sexual dysfunction because these agents are known to be useful in the treatment of sexual dysfunctions, including in female. Furthermore, it is known in the art that female sexual response is associated with vasodilation and engorgement of the genitalia with arterial blood. Therefore applying a composition containing known vasodilating agents, including the instant compounds directly onto any area of the genital would have been reasonably expected to be effective in causing vasodilatation and engorgement of the genitalia; and thereby treating female sexual dysfunction. Furthermore, incorporating known topical pharmaceutical composition excipients such as cyclodextrin, gelatin, and

hydroxypropyl methylcellulose such as hydroxypropyl methylcellulose 3000 (hydroxypropyl methylcellulose with a specific molecular weight) that are well known to be useful additives in forming topical compositions is considered within the skill of artisan.

Furthermroe, optimization of result effect parameters (e.g., the amount of ingredients such as hydroxymethylcellulose and misopriostol) is obvious as being within the skill of the artisan, absent evidence to the contrary.

Response to Arguments

Applicant's arguments filed June 7, 2004 with regard to the declaration filed by Dr. Panagiotis Kanakaris in March 8, 2004 have been fully considered but they are not persuasive. Dr. Kanakaris's declaration merely demonstrated that effectiveness of misoprostol against placebo. The experiment is not comparing the effectiveness of misoprostol against that of the closest prior art. The effectiveness of misoprostol in treating female sexual dysfunction comparing to placebo is considered as expected.

Applicant's arguments filed June 7, 2004 averring Buyuktimkin et al. have been considered moot as Buyuktimkin et al. is no longer cited in the rejection under 35 USC 103(a).

No new unanswered arguments is presented in the response filed June 7, 2004.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Patent Examiner
Art Unit 1617